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Set     Items   Description
S1        112   (PLASMODIUM(W)FALCIPARUM(W)ERYTHROCYTE(W)MEMBRANE(W)PROTEIN
              OR PFEMP1 OR PFEMP(W)1) (S) (BIND? OR ADHE?) AND (CHRONDROIT-
              IN(W)SULFATE(W)A OR CSA)
S2         23   RD (unique items)
?t2/3 ab/1-23
>>>No matching display code(s) found in file(s): 65, 165, 345

 2/AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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14665851   22561043   PMID: 12672527
  The 3D7var5.2 (var(COMMON)) type var gene family is commonly expressed in
non-placental Plasmodium falciparum malaria.
  Winter Gerhard; Chen Qijun; Flick Kirsten; Kremsner Peter; Fernandez
Victor; Wahlgren Mats
  Microbiology and Tumor Biology Center, Karolinska Institutet, P.O. Box
280, SE-171 77, Stockholm, Sweden
  Molecular and biochemical parasitology (Netherlands)  Apr 2003, 127
 (2) p179-91, ISSN 0166-6851   Journal Code: 8006324
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: In Process
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Searched by M. Smith

Relapse variants in chronic Plasmodium falciparum infections are antigenically distinct from the parental parasites. The variable antigen PfEMP1 expressed at the surface of the infected erythrocyte (IE) is encoded by the var gene family with approximately 60 copies per haploid genome. Placental isolates commonly express DBLgamma containing subtypes of var genes with homology to either 3D7var5.2 (var(COMMON)) or FCR3var(CSA). Here we report that var(COMMON) related genes are constitutively transcribed in approximately 60% of malaria infected children in Gabon. var(COMMON) is conserved in field isolates over at least 2.1kb. In 3D7 parasites var(COMMON) is present on chromosome 5 (var5.2) and constitutively transcribed in the opposite direction to most other var genes. It lacks a regulatory intron, an acidic terminal segment and ends in telomeric repeat sequences. var(COMMON) encodes a large, hypothetical PfEMP1 of a structure similar to previous placenta- binding PfEMP1s but it is not present at the IE-surface. IE of a 3D7 clone (3D7S8) transcribe var(COMMON) but express a PfEMP1 distinct from var(COMMON) at the surface and adhere to placental tissues through var(COMMON) independent novel mechanisms. Our report suggests that expression of var(COMMON) type genes is not restricted to placental malaria.

2/AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14408322 22451865 PMID: 12563735
Expression of Plasmodium falciparum-infected erythrocyte membrane protein from cerebral malaria patients.
Bian Z; Wang G; Tian X; Fan J
Department of Gastroenterology, Kunming General Hospital, Kunming 650032.
Zhongguo ji sheng chong xue yu ji sheng chong bing za zhi = Chinese journal of parasitology & parasitic diseases (China) 1999, 17 (6) p359-62, ISSN 1000-7423 Journal Code: 8709992
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process
AIM: To provide theoretical evidence for studying the molecular pathogenesis of human cerebral malaria. METHODS: The expressions of Plasmodium falciparum erythrocyte membrane protein 1(PfEMP1) on the surface of parasitized erythrocyte (PE) specimens from 19 cases of cerebral malaria patients in Yunnan Province were quantitatively analyzed by preparative sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) technique. 43 patients of falciparum malaria, 9 patients of vivax malaria and 6 healthy controls were also investigated. RESULTS: The expressions of higher molecular mass (Mr) 260-320 kDa forms of PfEMP1 were found on PE from cerebral malaria patients. By contrast, the expression of PfEMP1 and P. vivax erythrocyte membrane protein (PvEMP1) on PE from falciparum malaria patients and vivax malaria patients had a PfEMP1 with Mr 240 kDa and a PvEMP1 with Mr 180 kDa band, respectively. Healthy controls expressed an EMP of Mr 140 kDa. CONCLUSION: The binding of 260-320 kDa PfEMP1 proteins expressed on PE from cerebral malaria patients to diverse receptor molecules on the endothelial cell(EC) of the cerebral microvessels such as CD36, thrombospondin (TSP), intercellular adhesion molecule 1(ICAM-1), vascular cell adhesion molecule 1(VCAM-1), endothelial leukocyte adhesion molecule 1(ELAM-1) and chondroitin sulfate A (CSA) might be the molecular basis for the pathogenesis of cerebral malaria.

2/AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11568489 99000126 PMID: 9786187
A recombinant peptide based on PfEMP - 1 blocks and reverses adhesion of malaria-infected red blood cells to CD36 under flow.
Cooke B M; Nicoll C L; Baruch D I; Coppel R L
Department of Microbiology, Monash University, Clayton, Victoria, Australia. brian.cooke@med.monash.edu.au
Molecular microbiology (ENGLAND) Oct 1998, 30 (1) p83-90, ISSN 0950-382X Journal Code: 8712028
Contract/Grant No.: DK32094-10; DK; NIDDK
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
During falciparum malaria infection, severe complications ensue because parasitized red blood cells (PRBCs) adhere to endothelial cells and accumulate in the microvasculature. At the molecular level, adhesion is mediated by interaction of Plasmodium falciparum erythrocyte membrane protein 1 (PfEMP - 1) on the PRBC surface with receptors on the surface of endothelial cells, including CD36. We have shown that a recombinant 179-residue subfragment of PfEMP - 1 (rC1-2[1-179]), which encompasses the CD36- binding region, inhibits and reverses adhesion of PRBCs to CD36 under physiologically relevant flow conditions. rC1-2[1-179] inhibited adhesion in a concentration-dependent manner over the range 100 pM to 2 microM, with up to 99% of adhesion blocked at the highest concentration tested. The antiadhesive activity of rC1-2[1-179] was not strain specific and almost totally ablated adhesion of four different parasite lines. Furthermore, rC1-2[1-179] showed remarkable ability to progressively reverse adhesion when flowed over adherent PRBCs for 2h. The effect of rC1-2[1-179] was, however, specific for CD36-mediated adhesion and had no effect on adhesion mediated by CSA . Interference with binding of PRBCs to the vascular endothelium using rC1-2[1-179] or smaller organic mimetics may be a useful therapeutic approach to ameliorate severe complications of falciparum malaria.

2/AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10151246 22144028 PMID: 12149234
Sequestration of Plasmodium falciparum-infected erythrocytes to chondroitin sulfate A, a receptor for maternal malaria: monoclonal antibodies against the native parasite ligand reveal pan-reactive epitopes in placental isolates.
Lekana Douki Jean-Bernard; Traore Boubacar; Costa Fabio T M; Fusai Thierry; Pouvelle Bruno; Sterkers Yvon; Scherf Artur; Gysin Jurg
Unite de Parasitologie Experimentale, Faculte de Medecine, Universite de la Mediterranee (Aix-Marseille II), Marseille, France.
Blood (United States) Aug 15 2002, 100 (4) p1478-83, ISSN 0006-4971 Journal Code: 7603509
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Plasmodium falciparum parasites express variant adhesion molecules on the surface of infected erythrocytes (IEs), which act as targets for natural protection. Recently it was shown that IE sequestration in the placenta is mediated by binding to chondroitin sulfate A via the duffy binding -like (DBL)-gamma 3 domain of P falciparum erythrocyte membrane protein 1 (PfEMP1 (CSA)). Conventional immunization procedures rarely

result in the successful production of monoclonal antibodies (mAbs) against such conformational vaccine candidates. Here, we show that this difficulty can be overcome by rendering Balb/c mice B cells tolerant to the surface of human erythrocytes or Chinese hamster ovary (CHO) cells before injecting P falciparum IEs or transfected CHO cells expressing the chondroitin sulfate A (CSA)- binding domain (DBL-gamma 3) of the FCR3 var(CSA) gene. We fused spleen cells with P3U1 cells and obtained between 20% and 60% mAbs that specifically label the surface of mature infected erythrocytes of the CSA phenotype (mIE(CSA)) but not of other adhesive phenotypes. Surprisingly, 70.8% of the 43 mAbs analyzed in this work were IgM. All mAbs immunoprecipitated PfEMP1 (CSA) from extracts of (125)I surface-labeled IE(CSA). Several mAbs bound efficiently to the surface of CSA - binding parasites from different geographic areas and to placental isolates from West Africa. The cross-reactive mAbs are directed against the DBL-gamma 3(CSA), demonstrating that this domain, which mediates CSA binding , is able to induce a pan-reactive immune response. This work is an important step toward the development of a DBL-gamma 3-based vaccine that could protect pregnant women from pathogenesis.)

2/AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10144782 22133713 PMID: 12096191
Molecular basis for the dichotomy in Plasmodium falciparum adhesion to CD36 and chondroitin sulfate A.
Gamain Benoit; Gratepanche Sylvie; Miller Louis H; Baruch Dror I
Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892, USA. bgamain@niaid.nih.gov
Proceedings of the National Academy of Sciences of the United States of America (United States) Jul 23 2002, 99 (15) p10020-4, ISSN 0027-8424 Journal Code: 7505876
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Plasmodium falciparum-infected erythrocytes adhere dichotomously to the host receptors CD36 and chondroitin sulfate A (CSA). This dichotomy is associated with parasite sequestration to microvasculature beds (CD36) or placenta (CSA), leading to site-specific pathogenesis. Both properties are mediated by members of the variant P. falciparum erythrocyte membrane protein 1 (PfEMP - 1) family and reside on nonoverlapping domains of the molecule. To identify the molecular basis for the apparent dichotomy, we expressed various domains of PfEMP - 1 individually or in combination and tested their binding properties. We found that the CD36- binding mode of the cysteine-rich interdomain region-1 (CIDR1) ablates the ability of the Duffy binding -like gamma domain to bind CSA . In contrast, neither a non-CD36- binding CIDR1 nor an intercellular adhesion molecule 1 binding domain had any affect on CSA binding . Our findings point out that interactions between different domains of PfEMP - 1 can alter the adhesion phenotype of infected erythrocytes and provide a molecular basis for the apparent dichotomy in adhesion . We suggest that the basis for the dichotomy is structural and that mutually exclusive conformations of PfEMP - 1 are involved in binding to CD36 or CSA . Furthermore, we propose a model explaining the requirement for structural dichotomy between placental and nonplacental isolates.

2/AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10127685 22103453 PMID: 12106874
Two DBLgamma subtypes are commonly expressed by placental isolates of Plasmodium falciparum.
Fried Michal; Duffy Patrick E
Seattle Biomedical Research Institute, 4 Nickerson Street, WA 98109, USA. mfried@sbri.org
Molecular and biochemical parasitology (Netherlands) Jul 2002, 122 (2) p201-10, ISSN 0166-6851 Journal Code: 8006324
Contract/Grant No.: R01 AI43680; AI; NIAID; R01 AI48654; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Adhesion to chondroitin sulfate A (CSA), a distinguishing feature of malaria parasites obtained from the human placenta, might be mediated by the Duffy- binding -like (DBL) gamma domain of the variant surface antigen Plasmodium falciparum erythrocyte membrane protein -1 (PfEMP1). We studied transcription of var genes (that encode PfEMP1) in placental parasites by amplifying and sequencing DBLgamma fragments from genomic DNA and cDNA of field isolates collected in western Kenya. We amplified DBLgamma fragments with divergent sequences from individual isolates by using various sequence-specific or degenerate primers. Transcripts detected with degenerate primers clustered phylogenetically within two DBLgamma subtypes with homology to chr5 1.gen 150 or FCR3.varCSA. Interestingly, the DBLalpha encoded by chr5 1.gen 150 was recently found to be commonly expressed by placental isolates from Malawi (Mol. Biochem. Parasitol. 185 (2002) 1207). The findings are consistent with earlier serologic evidence that surface antigens of placental parasites have conserved features, and suggest that vaccines based on DBLgamma may only need to target a limited number of variants

2/AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09999357 21927235 PMID: 11930336
Identification of a conserved Plasmodium falciparum var gene implicated in malaria in pregnancy.
Rowe J Alexandra; Kyes Sue A; Rogerson Stephen J; Babiker Hamza A; Raza Ahmed
Institute of Cell, Animal, and Population Biology, University of Edinburgh, West Mains Road, Edinburgh EH9 3JT, United Kingdom. Alex.Rowe@ed.ac.uk
Journal of infectious diseases (United States) Apr 15 2002, 185 (8) p1207-11, ISSN 0022-1899 Journal Code: 0413675
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The Plasmodium falciparum erythrocyte membrane protein 1 (PfEMP1) family is a highly polymorphic class of variant surface antigens encoded by var genes that play an important role in malaria pathogenesis. This report describes the unexpected finding that 1 of the var genes encoding a PfEMP1 variant that binds to the host receptor chondroitin sulfate A (CSA) and is implicated in malaria in pregnancy is well conserved among P. falciparum isolates worldwide. The N-terminal domains of this PfEMP1 variant are especially highly conserved, whereas the functional CSA binding domain is more variable. Analysis of var gene expression in placental parasites from primigravid women in Malawi did not support a role

for this conserved gene in placental infection but identified a second commonly occurring var gene. These results indicate the need for reevaluation of previous assumptions of a minimal overlap between var gene repertoires from different parasite isolates.

2/AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09991383 21918495 PMID: 11918813
Transcription of multiple var genes by individual, trophozoite-stage Plasmodium falciparum cells expressing a chondroitin sulphate A binding phenotype.
Duffy Michael F; Brown Graham V; Basuki Wanny; Krejany Efrosinia O; Noviyanti Rintis; Cowman Alan F; Reeder John C
Australian Indonesia Medical Research Initiative (AusAID), Eijkman Institute for Molecular Biology, Eijkman Building, Jl. Diponegoro 69, Jakarta, Indonesia 10430. mduffy@unimelb.edu.au
Molecular microbiology (England) Mar 2002, 43 (5) p1285-93, ISSN 0950-382X Journal Code: 8712028
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
In this study, we detected multiple var gene transcripts within single, mature trophozoite-infected red blood cells (iRBCs) bound to chondroitin sulphate A (CSA). Several of the var detected had previously been demonstrated to encode Plasmodium falciparum erythrocyte membrane protein -1 (PfEMP - 1) variants with domains that mediated iRBC adhesion to receptors other than CSA . Parasites expressing the CSA - adherent phenotype transcribed far more of one var than of all others, but this gene was different from the two other var previously purported to encode adhesion to CSA . Previous work suggesting that only single var are transcribed by mature trophozoites needs re-examination in the light of these data from single, infected cells.

2/AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09751303 21554814 PMID: 11698301
Plasmodium falciparum erythrocyte membrane protein 1 functions as a ligand for P-selectin.
Senczuk A M; Reeder J C; Kosmala M M; Ho M
Department of Microbiology and Infectious Diseases and Immunology Research Group, University of Calgary, Calgary, Alberta, Canada.
Blood (United States) Nov 15 2001, 98 (10) p3132-5, ISSN 0006-4971 Journal Code: 7603509
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The malarial protein Plasmodium falciparum erythrocyte membrane protein 1 (PfEMP1) is a parasite protein that is exported to the surface of the infected erythrocyte, where it is inserted into the red cell cytoskeleton in the second half of the parasite life cycle. The surface expression of PfEMP1 coincides with the occurrence of the adhesion of infected erythrocytes to vascular endothelium. This protein has been shown to interact with CD36, intercellular adhesion molecule-1 (ICAM-1) and chondroitin sulfate A (CSA). In this study, it is demonstrated by

affinity purification and western blot analysis that PfEMP1 also functions as a cell surface ligand for P-selectin, an adhesion molecule that has been shown to mediate the rolling of infected erythrocytes under physiologic flow conditions, leading to a significant increase in adhesion to CD36 on activated platelets and microvascular endothelium.

2/AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09466889 21240434 PMID: 11342458
Modifications in the CD36 binding domain of the Plasmodium falciparum variant antigen are responsible for the inability of chondroitin sulfate A adherent parasites to bind CD36.
Gamain B; Smith J D; Miller L H; Baruch D I
Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA.
Blood (United States) May 15 2001, 97 (10) p3268-74, ISSN 0006-4971 Journal Code: 7603509
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Adhesion of mature Plasmodium falciparum parasitized erythrocytes to microvascular endothelial cells or to placenta contributes directly to the virulence and severe pathology of P falciparum malaria. Whereas CD36 is the major endothelial receptor for microvasculature sequestration, infected erythrocytes adhering in the placenta bind chondroitin sulfate A (CSA) but not CD36. Binding to both receptors is mediated by different members of the large and diverse protein family P falciparum erythrocyte membrane protein-1 (PfEMP - 1) and involves different regions of the molecule. The PfEMP - 1 - binding domain for CD36 resides in the cysteine-rich interdomain region 1 (CIDR-1). To explore why CSA - binding parasites do not bind CD36, CIDR-1 domains from CD36- or CSA - binding parasites were expressed in mammalian cells and tested for adhesion . Although CIDR-1 domains from CD36- adherent strains strongly bound CD36, those from CSA - adherent parasites did not. The CIDR-1 domain has also been reported to bind CSA . However, none of the CIDR-1 domains tested bound CSA . Chimeric proteins between CIDR-1 domains that bind or do not bind CD36 and mutagenesis experiments revealed that modifications in the minimal CD36- binding region (M2 region) are responsible for the inability of CSA -selected parasites to bind CD36. One of these modifications, mapped to a 3-amino acid substitution in the M2 region, ablated binding in one variant and largely reduced binding of another. These findings provide a molecular explanation for the inability of placental sequestered parasites to bind CD36 and provide additional insight into critical residues for the CIDR-1/CD36 interaction.

2/AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09395407 21160699 PMID: 11260135
Molecular mechanisms of Plasmodium falciparum placental adhesion.
Scherf A; Pouvelle B; Buffet P A; Gysin J
Unite de Biologie des Interactions Hote-Parasite, CNRS URA 1960, Institut Pasteur, 25 rue du Dr Roux, 75724 Paris, France. ascherf@pasteur.fr
Cellular microbiology (England) Mar 2001, 3 (3) p125-31, ISSN 1462-5814 Journal Code: 100883691
Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

In natural Plasmodium falciparum infections, parasitized erythrocytes (PEs) circulate in the peripheral blood for a period corresponding roughly to the first part of the erythrocytic life cycle (ring stage). Later, in blood-stage development, parasite-encoded adhesion molecules are inserted into the erythrocyte membrane, preventing the circulation of the PEs. The principal molecule mediating PE adhesion is P. falciparum erythrocyte membrane protein 1 (PfEMP1), encoded by the polymorphic var gene family. The population of parasites is subject to clonal antigenic variation through changes in var expression, and a single PfEMP1 variant is expressed at the PE surface in a mutually exclusive manner. In addition to its role in immune evasion, switches in PfEMP1 expression may be associated with fundamental changes in parasite tissue tropism in malaria patients. A switch from CD36 binding to chondroitin sulphate A (CSA) binding may lead to extensive sequestration of PEs in placenta syncytiotrophoblasts. This is probably a key event in malaria pathogenesis during pregnancy. The CSA - binding phenotype of mature PEs is linked to another distinct adhesive phenotype: the recently described CSA -independent cytoadhesion of ring-stage PEs. Thus, a subpopulation of PEs that sequentially displays these two different phenotypes may bind to an individual endothelial cell or syncytiotrophoblast throughout the asexual blood-stage cycle. This suggests that non-circulating (cryptic) parasite subpopulations are present in malaria patients.

2/AB/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09373777 21136462 PMID: 11237850

Variants of Plasmodium falciparum erythrocyte membrane protein 1 expressed by different placental parasites are closely related and adhere to chondroitin sulfate A.

Khattab A; Kun J; Deloron P; Kremsner P G; Klinkert M Q
Department of Parasitology, Institute for Tropical Medicine, University of Tubingen, Tubingen, Germany.

Journal of infectious diseases (United States) Apr 1 2001, 183 (7) p1165-9, ISSN 0022-1899 Journal Code: 0413675
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Plasmodium falciparum-infected erythrocytes adhere to syncytiotrophoblast cells lining the placenta via glycosaminoglycans, such as chondroitin sulfate A (CSA) and hyaluronic acid. Adherence of infected erythrocytes to host receptors is mediated by P. falciparum erythrocyte membrane protein-1 (PfEMP - 1). A single PfEMP - 1 domain (duffy binding -like [DBL]-3, of the gamma sequence class) from laboratory-adapted strains is thought to be responsible for binding to CSA . In this study, DBL-gamma domains expressed by placental P. falciparum isolates were shown to have an affinity to CSA . All parasite populations accumulating in infected placentas express only 1 variant of PfEMP - 1 , each of which contains a DBL-gamma domain with CSA binding capacities. Furthermore, sequence analysis data provide evidence for antigenic conservation among the DBL-gamma sequences expressed by different placental parasites. This study offers a close reflection of the process of parasite adhesion in the placenta and is crucial to the understanding of the pathogenesis of malaria during pregnancy.

2/AB/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09208141 20517637 PMID: 11062539
Cytoadhesion of Plasmodium falciparum ring-stage-infected erythrocytes.
Pouvelle B; Buffet P A; Lepolard C; Scherf A; Gysin J
Laboratoire de Parasitologie Experimentale, Faculte de Medecine, Universite de la Mediterranee (Aix-Marseille II), 13385 Marseille Cedex 5, France.
Nature medicine (UNITED STATES) Nov 2000, 6 (11) p1264-8, ISSN 1078-8956 Journal Code: 9502015
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A common pathological characteristic of Plasmodium falciparum infection is the cytoadhesion of mature-stage-infected erythrocytes (IE) to host endothelium and syncytiotrophoblasts. Massive accumulation of IE in the brain microvasculature or placenta is strongly correlated with severe forms of malaria. Extensive binding of IE to placental chondroitin sulfate A (CSA) is associated with physiopathology during pregnancy. The adhesive phenotype of IE correlates with the appearance of Plasmodium falciparum erythrocyte membrane protein 1 (PfEMP1) at the erythrocyte surface (approximately 16 h after merozoite invasion), so that only early blood-stage (ring-stage) IE appear in the peripheral blood. Here, we describe results that challenge the existing view of blood-stage IE biology by demonstrating the specific adhesion of IE, during the early ring-stage, to endothelial cell lines from the brain and lung and to placental syncytiotrophoblasts. Later, during blood-stage development of these IE, trophozoites switch to an exclusively CSA cytoadhesion phenotype. Therefore, adhesion to an individual endothelial cell or syncytiotrophoblast may occur throughout the blood-stage cycle, indicating the presence in malaria patients of noncirculating (cryptic) parasite subpopulations. We detected two previously unknown parasite proteins on the surface of ring-stage IE. These proteins disappear shortly after the start of PfEMP1 -mediated adhesion .

2/AB/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09022396 20316015 PMID: 10858204
Identification of glycosaminoglycan binding domains in Plasmodium falciparum erythrocyte membrane protein 1 of a chondroitin sulfate A- adherent parasite.
Reeder J C; Hodder A N; Beeson J G; Brown G V
Walter and Eliza Hall Institute of Medical Research, Parkville, Victoria 3050, Australia. imrgka@datec.com.pg
Infection and immunity (UNITED STATES) Jul 2000, 68 (7) p3923-6, ISSN 0019-9567 Journal Code: 0246127
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Accumulation of Plasmodium falciparum-infected erythrocytes in the placenta is a key feature of maternal malaria. This process is mediated in part by the parasite ligand P. falciparum erythrocyte membrane protein 1 (PfEMP1) at the surface of the infected erythrocyte interacting with the host receptor chondroitin sulfate A (CSA) on the placental lining. We have localized CSA binding activity to two adjacent domains in PfEMP1

of an adherent parasite line and shown the presence of at least three active glycosaminoglycan binding sites. A putative CSA binding sequence was identified in one domain, but nonlinear binding motifs are also likely to be present, since binding activity in the region was shown to be dependent on conformation. Characterization of this binding region provides an opportunity to investigate further its potential as a target for antiadhesion therapy.

2/AB/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08973502 20264023 PMID: 10802316
Characterisation of the chondroitin sulphate of Saimiri brain microvascular endothelial cells involved in Plasmodium falciparum cytoadhesion.
Fusai T; Parzy D; Spillmann D; Eustacchio F; Pouvelle B; Lepolard C; Scherf A; Gysin J
Unite de Parasitologie, IMTSSA, Boulevard Charles Livon, Jardin du Pharo, 13007, Marseille, France.
Molecular and biochemical parasitology (NETHERLANDS) Apr 30 2000, 108 (1) p25-37, ISSN 0166-6851 Journal Code: 8006324
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Cytoadhesion of Plasmodium falciparum-infected erythrocytes (IRBC) to chondroitin-4-sulphate (CSA) is inhibited by soluble CSA in vitro on Saimiri brain microvascular endothelial cells (SBEC) and in vivo in P. falciparum-infected Saimiri monkeys. We tested whether the SBEC model was appropriate for studying CSA - binding IRBC using four cell lines. All SBEC expressed a chondroitin sulphate (CS), with a composition of CSA . The mean sizes of these CSA were 20.5, 22, 23, 32.5 and 36 kDa for SBEC 3A and C2, CHO, SBEC 1D and 17, respectively. We found that cytoadhesion of the Palo-Alto (FUP)1 CSA - binding phenotype, selected by panning on SBEC 17, was specifically inhibited in a dose-dependent manner by all the purified CSA . The extent of inhibition depended on the cellular origin of the tested CSA . SBEC 17 CSA was 33 times more efficient than CHO- CSA and 21 times more efficient than the 50 kDa commercial bovine trachaea CSA . Dynabeads coated with a total extract of SBEC 1D CS-proteoglycans interacted with CSA - but not with CD36- or ICAM-1- binding IRBC. These Dynabeads also interacted specifically with the PfEMP1 DBL-3 domain, on the surface of CHO transfectants, but not with the CIDR-1 domain. Thrombomodulin was involved in IRBC adhesion to all SBEC whereas CD44 was only expressed by SBEC 1D and 17. These two CSA -proteoglycans have also been detected at the surface of human endothelial cells. Thus, the two homologous models, SBEC/Saimiri sciureus, are useful and reliable tools for the evaluation of new anti- CSA adhesion treatments and anti-disease vaccines for pregnant women.

2/AB/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08727002 20006305 PMID: 10535993
Plasmodium falciparum domain mediating adhesion to chondroitin sulfate A: a receptor for human placental infection.
Buffet P A; Gamain B; Scheidig C; Baruch D; Smith J D; Hernandez-Rivas R; Pouvelle B; Oishi S; Fujii N; Fusai T; Parzy D; Miller L H; Gysin J; Scherf A

Unite de Biologie des Interactions Hote-Parasite, Centre National de la Recherche Scientifique/Unite de Recherche Associee 1960, Institut Pasteur, 75724 Paris, France.

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Oct 26 1999, 96 (22) p12743-8, ISSN 0027-8424
Journal Code: 7505876
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
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Malaria during the first pregnancy causes a high rate of fetal and neonatal death. The decreasing susceptibility during subsequent pregnancies correlates with acquisition of antibodies that block binding of infected red cells to chondroitin sulfate A (CSA), a receptor for parasites in the placenta. Here we identify a domain within a particular Plasmodium falciparum erythrocyte membrane protein 1 that binds CSA . We cloned a var gene expressed in CSA - binding parasitized red blood cells (PRBCs). The gene had eight receptor-like domains, each of which was expressed on the surface of Chinese hamster ovary cells and was tested for CSA binding . CSA linked to biotin used as a probe demonstrated that two Duffy- binding -like (DBL) domains (DBL3 and DBL7) bound CSA . DBL7, but not DBL3, also bound chondroitin sulfate C (CSC) linked to biotin, a negatively charged sugar that does not support PRBC adhesion . Furthermore, CSA , but not CSC, blocked the interaction with DBL3; both CSA and CSC blocked binding to DBL7. Thus, only the DBL3 domain displays the same binding specificity as PRBCs. Because protective antibodies present after pregnancy block binding to CSA of parasites from different parts of the world, DBL-3, although variant, may induce cross-reactive immunity that will protect pregnant women and their fetuses.

2/AB/17 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13348021 BIOSIS NO.: 200100555170
Pathophysiology of gestational malaria.
ORIGINAL LANGUAGE TITLE: Pathogenie du paludisme gestationnel.
AUTHOR: Buffet Pierre A; Scherf Artur(a)
AUTHOR ADDRESS: (a)Unite de Biologie des Interactions Hote-Parasite, CNRS URA 1960, Institut Pasteur, 25, Rue du Docteur-Roux, 75724, Paris Cedex 15: ascherf@pasteur.fr**France
JOURNAL: M-S (Medecine Sciences) 17 (10):p1017-1026 Octobre, 2001
MEDIUM: print
ISSN: 0767-0974
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: French; Non-English
SUMMARY LANGUAGE: English; French

ABSTRACT: Malaria during first pregnancy causes disease in both mother and fetus in hyperendemic areas even in women who were previously immune. Our understanding of the factors leading to this clinical form has progressed considerably during the last years. Gestational malaria is strongly associated with the sequestration of P. falciparum-infected erythrocytes to the placental glycosaminoglycan chondroitin sulfate A (CSA) via a parasite derived variant adhesion surface molecule, called PfEMP1 . A specific PfEMP1 domain has been identified in our laboratoy that mediates binding to CSA of placenta syncytiotrophoblasts: This domain is a candidate as a vaccine for pregnant women in Africa. Studies on parasite sequestration have led to the discovery of two other parasite molecules exposed on the surface of infected erythrocytes probably

involed in the adhesion to syncytiotrophoblasts during the entire 48 hours blood stage cycle.

DESCRIPTORS:
2001

2/AB/18 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12640757 BIOSIS NO.: 200000394259
Plasmodium falciparum: Cloned and expressed CIDR domains of PfEMP1 bind to chondroitin sulfate A.
AUTHOR: Degen Roland(a); Weiss Niklaus(a); Beck Hans-Peter(a)
AUTHOR ADDRESS: (a)Swiss Tropical Institute, CH 4002, Basel**Switzerland
JOURNAL: Experimental Parasitology 95 (2):p113-121 June, 2000
MEDIUM: print
ISSN: 0014-4894
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Adherence of erythrocytes infected with mature asexual Plasmodium falciparum parasites (iRBC) to microvascular endothelial cells contributes to the pathology of P. falciparum malaria. It has been shown that the variant P. falciparum erythrocyte membrane protein 1 (PfEMP1) confers adhesion to a wide range of cell surface receptors. Previously, the cysteine-rich interdomain region (CIDR) of PfEMP1 has been identified as binding site to CD36. We provide evidence that the same region can also mediate binding to chondroitin sulfate A (CSA). CIDR domains of two different parasite strains were expressed in Escherichia coli as a 6xHis-tagged protein. Purified recombinant protein bound to Chinese hamster ovary (CHO) cells which naturally express chondroitin sulfate A. Treatment of wild-type CHO cells with chondroitinase ABC reduced binding up to 94.4%. Competitive binding using soluble CSA inhibited binding to CHO cells by up to 100% at 2 mg/ml and by 62.4% at 0.5 mg/ml, whereas 1 mg/ml heparan sulfate had only a little effect (18.1%). In contrast, a recombinant 6xHis-tagged DBL1 domain showed no binding to wild-type CHO cells. Such an approach of analyzing various domains of PfEMP1 as recombinant proteins may elucidate their functions and may lead to novel anti- adherence therapeutics, especially for maternal malaria infections.

2000

2/AB/19 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

10899763 Genuine Article#: 582RG Number of References: 28
Title: Sequestration of Plasmodium falciparum-infected erythrocytes to chondroitin sulfate A, a receptor for maternal malaria: monoclonal antibodies against the native parasite ligand reveal pan-reactive epitopes in placental isolates (ABSTRACT AVAILABLE)
Author(s): Douki JBL; Traore B; Costa FTM; Fusai T; Pouvelle B; Sterkers Y; Scherf A; Gysin J (REPRINT)
Corporate Source: Univ Mediterranee,Fac Med, Unite Parasitol Expt, URA IPP IMTSSA,EA3282/F-13385 Marseille 5//France/ (REPRINT); Univ Mediterranee,Fac Med, Unite Parasitol Expt, URA IPP IMTSSA,F-13385

Marseille 5//France/; Inst Pasteur,Unite Biol Interact Hote Parasite,Paris//France/
Journal: BLOOD, 2002, V100, N4 (AUG 15), P1478-1483
ISSN: 0006-4971 Publication date: 20020815
Publisher: AMER SOC HEMATOLOGY, 1900 M STREET. NW SUITE 200, WASHINGTON, DC 20036 USA
Language: English Document Type: ARTICLE
Abstract: Plasmodium falciparum parasites express variant adhesion molecules on the surface of infected erythrocytes (IEs), which act as targets for natural protection. Recently it was shown that IE sequestration in the placenta is mediated by binding to chondroitin sulfate A via the duffy binding -like (DBL)-gamma3 domain of P falciparum erythrocyte membrane protein 1 (PfEM1(CSA)). Conventional immunization procedures rarely result in the successful production of monoclonal antibodies (mAbs) against such conformational vaccine candidates. Here, we show that this difficulty can be overcome by rendering Balb/c mice B cells tolerant to the surface of human erythrocytes or Chinese hamster ovary (CHO) cells before injecting P falciparum, IEs or transfected CHO cells expressing the chondroltin sulfate A (CSA)- binding domain (DBL-gamma3) of the FCR3 var(CSA) gene. We fused spleen cells with P3U1 cells and obtained between 20% and 60% mAbs that specifically label the surface of mature infected erythrocytes of the CSA phenotype (mIE(CSA)) but not of other adhesive phenotypes. Surprisingly, 70.8% of the 43 mAbs analyzed in this work were IgM. All mAbs immunoprecipitated PfEMP1 (CSA) from extracts of I-125 surface-labeled IECSA. Several mAbs bound efficiently to the surface of CSA - binding parasites from different geographic areas and to placental isolates from West Africa. The cross-reactive mAbs are directed against the DBL-gamma3(CSA), demonstrating that this domain, which mediates CSA binding , is able to Induce a pan-reactive immune response. This work is an important step toward the development of a DBL-gamma3-based vaccine that could protect pregnant women from pathogenesis. (C) 2002 by The American Society of Hematology.

2/AB/20 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

10751387 Genuine Article#: 564KM Number of References: 35
Title: The structural motif in chondroitin sulfate for adhesion of Plasmodium falciparum-infected erythrocytes comprises disaccharide units of 4-O-sulfated and non-sulfated N-acetylgalactosamine linked to glucuronic acid (ABSTRACT AVAILABLE)
Author(s): Chai WG (REPRINT) ; Beeson JG; Lawson AM
Corporate Source: Northwick Pk Hosp & Clin Res Ctr,Imperial Coll Sch Med, MRC, Glycosci Lab,Harrow HA1 3UJ/Middx/England/ (REPRINT); Northwick Pk Hosp & Clin Res Ctr,Imperial Coll Sch Med, MRC, Glycosci Lab,Harrow HA1 3UJ/Middx/England/; Univ Melbourne,Royal Melbourne Hosp, Dept Med,Parkville/Vic 3050/Australia/
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, 2002, V277, N25 (JUN 21), P 22438-22446
ISSN: 0021-9258 Publication date: 20020621
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA
Language: English Document Type: ARTICLE
Abstract: An important characteristic of malaria parasite Plasmodium falciparum-infected red blood cells (IRBCs) is their ability to adhere to host endothelial cells and accumulate in various organs. Sequestration of IRBCs in the placenta, associated with excess perinatal and maternal mortality, is mediated in part by adhesion of

parasites to the glycosaminoglyean chondroitin sulfate A (CSA) present on sncytiotrophoblasts lining the placental blood spaces. To define key structural features for parasite interactions, we isolated from CSA oligosaccharide fractions and established by electrospray mass spectrometry and high performance liquid chromatography disaccharide composition analysis their differing chain length, sulfate content, and sulfation pattern. Testing these defined oligosaccharide fragments for their ability to inhibit IRBC adhesion to immobilized CSA revealed the importance of non-sulfated disaccharide units in combination with 4-O-sulfated disaccharides for interaction with IRBCs. Selective removal of 6-O-sulfates from oligo- and polysaccharides to increase the proportion of non-sulfated disaccharides enhanced activity, indicating that 6-O-sulfation interferes with the interaction of CSA with IRBCs. Dodecasaccharides with four or five 4-O-sulfated and two or one non-sulfated disaccharide units, respectively, comprise the minimum chain length for effective interaction with IRBCs. Comparison of the activities of CSA and CSB oligo- and polysaccharides with a similar sulfation pattern and content achieved from partial desulfation demonstrated that glucuronic acid rather than iduronic acid residues are important for IRBC binding.

2/AB/21 (Item 1 from file: 50)
DIALOG(R)File 50:CAB Abstracts

04074823 CAB Accession Number: 20013097011
Parasite adhesion and immune evasion in placental malaria.
Beeson, J. G.; Reeder, J. C.; Rogerson, S. J.; Brown, G. V.
Dept of Medicine, University of Melbourne, Royal Melbourne Hospital, Parkville, VIC 3050, Australia.
Trends in Parasitology vol. 17 (7): p.331-337
Publication Year: 2001
ISSN: 1471-4922 --
Language: English
Document Type: Journal article
This review focuses on 3 key parasite determinants of Plasmodium falciparum infection of the placenta: (1) the emergence of novel parasite variants or serotypes in pregnancy, which are able to evade pre-existing immunity; (2) adhesion of P. falciparum-infected erythrocytes to glycosaminoglycans lining placental blood spaces (e.g. chondroitin sulfate A (CSA) and hyaluronic acid (HA)); and (3) the expression of var genes encoding the parasite protein P. falciparum erythrocyte membrane protein 1 (PfEMP1), which is important in determining the antigenic and adhesive phenotypes of infected erythrocytes. 65 ref.

2/AB/22 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

15569214 PASCAL No.: 02-0269629
Molécules de surface de l'hematie parasitee par Plasmodium falciparum impliquees dans la physiopathologie du paludisme gestationnel
(Surface molecules of Plasmodium falciparum-infected erythrocytes involved in the pathophysiology of gestational malaria)
BUFFET Pierre; SCHERF Artur, dir
Universite de Paris 07, Paris, France
Univ.: Universite de Paris 07. Paris. FRA Degree: Th. doct.
2000-12; 2000 167 p.
Language: French Summary Language: French; English
L' adherence des hematies parasitees par P. falciparum (HP) a des

recepteurs endotheliaux humains est un element cle de la physiopathologie du paludisme. La sequestration des HP pendant la deuxieme moitie du cycle intra-erythrocytaire est liee a l'expression de la proteine parasitaire polymorphe PfEMP1 (specifiee par la famille multigenique var). La sequestration placentaire des HP pendant la premiere grossesse, par adherence sur la chondroitine sulfate A (CSA), permet la proliferation d'un nouveau variant antigenique. Ce paludisme gestationnel entraine une anemie maternelle et une mortalite infantile accrue. La selection in vitro de populations parasitaires isogeniques de phenotype de cytoadherence defini, nous a permis de montrer que la regulation d'expression de la famille var est epigenetique (commutation in situ), et que le controle transcriptionnel en deuxieme moitie de cycle est mutuellement exclusif : une population de phenotype defini n'exprime qu'un seul gene var. Le ligand proteique exprime par une population adherant exclusivement a la CSA , est un membre unique de la famille PfEMP1 . L'expression des 8 domaines de cette proteine a la surface de cellules CHO a permis d'identifier le domaine implique dans l'interaction avec la CSA : le DBL3 gamma . Nous avons participe a la description recente de la cytoadherence d'HP en premiere moitie de cycle. Ce nouveau phenotype, bien que lie a la cytoadherence des HP sur la CSA en deuxieme moitie de cycle, est opere par un couple recepteur endothelial/ligand parasitaire encore inconnu. Deux nouvelles proteines parasitaires immunogenes, presentes a la surface des HP uniquement en premiere moitie de cycle (RSP-1 et RSP-2) sont les operateurs putatifs de la cytoadherence en premiere moitie de cycle et expliqueraient la discordance entre les densites parasitaires placentaire (elevee) et peripherique (faible ou nulle) pendant la grossesse. Ces resultats font esperer le developpement d'un vaccin contre le paludisme gestationnel.

2/AB/23 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

13238124 PASCAL No.: 97-0507527
Acces palustres graves chez l'homme: Contribution a l'etude in vitro du mecanisme physiopathologique de la sequestration
(Sequestration of P. falciparum-infected red blood cell as a pathophysiological mecanism of human complicated malaria)
MUANZA Kabongo; GENTILINI M, dir
Universite de Paris 06, Paris, Francee
Univ.: Universite de Paris 06. Paris. FRA Degree: Th. doct.
1996-02; 1996 178 p.
Language: French Summary Language: French; English
Parmi plusieurs mecanismes physiopathologiques complexes impliques dans la pathogenese des formes compliquees des acces de paludisme a Plasmodium falciparum, la sequestration des hematies parasitees par les formes matures de P. falciparum dans les microvaisseaux est probablement a la base de la maladie vasoocclusive et metabolique dans les organes-cibles. L'utilisation de differents modeles d'etude in vitro (HUVECs, cellules C32 et cellules CHO et COS transfectees avec CD36 et ICAM-1) a permis d'identifier et de caracteriser les differents recepteurs d' adherence comprenant CD36, ICAM-1, la Thrombospondine, E-selectine, VCAM-1 et plus recemment la Chondroitine-4-sulfate. Les cytokines jouent un role dans la modulation de certains de ces recepteurs. Quant aux ligands parasitaires, les genes codant pour PfEMP1 ont ete caracterises ; ce qui ouvre des perspectives dans la comprehension de la sequestration au niveau moleculaire. Le tropisme visceral de Plasmodium est variable et ubiquitaire. La connaissance de differents patterns des recepteurs exprimes dans les differents tissus-cibles est indispensable a la fois pour la comprehension de la physiopathologie et dans la mise au point des strategies plus

efficaces d'une eventuelle therapie anti-sequestration. Notre travail procede de cette demarche. Nous avons d'abord mis au point une technique efficace et fiable pour l'isolement des cellules endotheliales des microvaisseaux pulmonaires humains (HLECs) pour ensuite nous consacrer a la mise au point d'un modele in vitro d'etude de la cytoadherence d'un organe cible de P. falciparum, le poumon humain. Ce modele presente l'avantage d'etre tres proche des conditions physiologiques en ce qui concerne l'expression des recepteurs potentiels de la cytoadherence. L'expression de certains recepteurs est modulee par des cytokines. In vivo la chondroitine-4-sulfate (CSA) exprimee a la surface des cellules endotheliales cerebrales du Saimiri sciureus a ete recemment decrite comme un nouveau recepteur de la cytoadherence. L'etude complementaire de caracterisation de ce recepteur sur notre modele a permis de confirmer chez l'homme, a l'instar de ce qui a ete observe chez le singe, la presence de ce nouveau recepteur. L'utilisation d'anticorps specifiques diriges contre ce recepteur a permis d'inhiber de facon specifique l' adherence aux HLECs de plusieurs souches de laboratoire capables d'infecter le singe. Les HLEC constituent donc un systeme multipotent et sont capables de se lier aux adhesines via l'un ou l'autre des 5 recepteurs (tels que CD36, ICAM-1, E-selectine, VCAM-1 et chondroitine-4-sulfate), probablement en fonction de variations du couple affinite/avidite en rapport avec la souche plasmodiale en cause. Ce modele est en cours d'exploitation dans les etudes in vitro des acces palustres graves de l'homme, en vue de determiner les facteurs de virulence de souches, les interactions entre le paludisme et le VIH et les effets directs du parasite sur les cellules endotheliales humaines en coculture

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=> d stat que
L1            10 SEA FILE=REGISTRY ("PLASMODIUM FALCIPARUM ASPARAGINE-RICH
                 PROTEIN (PLASMODIUM FALCIPARUM STRAIN 3D7 GENE MAL13P1.63)"/CN
                 OR "PLASMODIUM FALCIPARUM CIRCUMSPOROZOITE HELPER T CELL
                 EPITOPE"/CN OR "PLASMODIUM FALCIPARUM ERYTHROCYTE MEMBRANE
                 PROTEIN"/CN OR "PLASMODIUM FALCIPARUM GAMETE ANTIGEN 27/25
                 (PLASMODIUM FALCIPARUM STRAIN 3D7 GENE PF13_0011)"/CN OR
                 "PLASMODIUM FALCIPARUM MEMBRANE PROTEIN PF12 PRECURSOR
                 (PLASMODIUM FALCIPARUM STRAIN 3D7 GENE MAL6P1.299)"/CN OR
                 "PLASMODIUM FALCIPARUM MSP8-LIKE PROTEIN (PLASMODIUM FALCIPARUM
                  STRAIN 3D7 GENE MAL6P1.221)"/CN OR "PLASMODIUM FALCIPARUM
                 PROTEIN KINASE (PLASMODIUM FALCIPARUM STRAIN 3D7 CLONE MAL4P3
                 GENE PFD0740W)"/CN OR "PLASMODIUM FALCIPARUM RETICULOCYTE
                 BINDING PROTEIN 2 B (PLASMODIUM FALCIPARUM STRAIN 3D7 GENE
                 MAL13P1.176)"/CN OR "PLASMODIUM FALCIPARUM TROPHOZOITE ANTIGEN
                 R45-LIKE PROTEIN (PLASMODIUM FALCIPARUM STRAIN 3D7 CLONE
                 MAL4P4 GENE PFD1175W)"/CN OR "PLASMODIUM KNOWLESI ACID
                 ENDOPEPTIDASE"/CN OR "PLASMODIUM-SPECIFIC HYDROPHOBIC ABUNDANT
                 PROTEIN (PHYSARUM POLYCEPHALUM CLONE GLAV1-1 PRECURSOR)"/CN)
L2             7 SEA FILE=REGISTRY "PFEMP-1, TRUNCATED (PLASMODIUM FALCIPARUM
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                  GENE PFB0045C)"/CN OR "PFEMP1 (PLASMODIUM FALCIPARUM GENE
                 PFB1055C)"/CN OR "PFEMP1 FRAGMENT (PLASMODIUM FALCIPARUM GENE
                 PFB1045W)"/CN OR "PFEMP1-LIKE PROTEIN (PLASMODIUM FALCIPARUM
                 STRAIN 3D7 GENE MAL6P1.312)"/CN OR "PFEMP1-LIKE PROTEIN,
                 TRUNCATED (PLASMODIUM FALCIPARUM STRAIN 3D7 GENE MAL6P1.312)"/C
                 N)
L4             2 SEA FILE=REGISTRY FCR3(L)VAR(L)CSA
L5           147 SEA FILE=HCAPLUS L1 OR L2 OR PLASMODIUM(W)FALCIPARUM(W)ERYTHROC
                 YTE(W)MEMBRANE(W)PROTEIN OR PFEMP1 OR PFEMP(W)1
L7             3 SEA FILE=HCAPLUS L4 OR FCR3(L)VAR(L)CSA
L9             3 SEA FILE=HCAPLUS L5 AND L7
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=> d ibib abs hitrn 19 1-3

L9 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:576698 HCAPLUS
DOCUMENT NUMBER: 137:305633
TITLE: A distinct 5' flanking var gene region regulates Plasmodium falciparum variant erythrocyte surface antigen expression in placental malaria
AUTHOR(S): Vazquez-Macias, Aleida; Martinez-Cruz, Perla; Castaneda-Patlan, Maria Cristina; Scheidig, Christine; Gysin, Jurg; Scherf, Artur; Hernandez-Rivas, Rosaura
CORPORATE SOURCE: Department of Molecular Biomedicine, Centro de Investigacion y de Estudios Avanzados del IPN, Mexico, Mex.
SOURCE: Molecular Microbiology (2002), 45(1), 155-167
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The Plasmodium falciparum multigene **var** family codes for approx. 50 variant adhesive proteins expressed in a mutually exclusive manner at the surface of infected red blood cells (iRBCs). Switching expression of **var** genes can lead to fundamental changes in the adhesive and antigenic properties of iRBCs. For example, a specific phenotypic switch in adhesion from CD36 to chondroitin sulfate A (**CSA**) is assocd. with malaria pathogenesis in pregnant women. The factors and DNA elements that control the expression of a particular member of the **var** gene family during gestational malaria remains enigmatic. Here, the authors report that the subtelomeric **FCR3** varCSA is expressed under the control of a unique DNA element of 1.8 kb, whereas the other members of the **var** multigene family are flanked by common regulatory elements. The 5' varCSA-type element is conserved as a single copy in lab. strains and clin. isolates from Brazil and West Africa and contains two distinct repetitive elements of 150 bp and 60 bp resp. The 5' varCSA-type sequence tags a **var** gene in the 3D7 genome that is homologous to the **FCR3** varCSA gene. A recombinant DBL.gamma. domain of this **var** gene showed specific binding to **CSA** . This subtelomeric varCSA gene is transcribed in the opposite sense when compared with the usual orientation of telomere-adjacent **var** genes. This unique arrangement might explain why the varCSA gene is relatively conserved in genetically distinct parasites despite being located in a highly recombinogenic chromosome compartment. The 5' untranslated region (UTR) of the varCSA-type sequence is also transcribed in placental isolates that bind to **CSA**, illustrating an important role for the unique 5' varCSA-type sequence in the regulation of **var** genes involved in malaria pathogenesis in pregnant women. However, this promoter is not always transcribing **var** genes selected for expression of products that bind to **CSA** in vitro. The work identifies a sequence tag for the identification of varCSA genes in placental isolates for the first time.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:509983 HCAPLUS
DOCUMENT NUMBER: 137:350349
TITLE: Two DBL.gamma. subtypes are commonly expressed by placental isolates of Plasmodium falciparum
AUTHOR(S): Fried, Michal; Duffy, Patrick E.

CORPORATE SOURCE: Seattle Biomedical Research Institute, Seattle, WA, 98109, USA
SOURCE: Molecular and Biochemical Parasitology (2002), 122(2), 201-210
CODEN: MBIPDP; ISSN: 0166-6851
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Adhesion to chondroitin sulfate A (**CSA**), a distinguishing feature of malaria parasites obtained from the human placenta, might be mediated by the Duffy-binding-like (DBL) .gamma. domain of the variant surface antigen **Plasmodium falciparum erythrocyte membrane protein**-1 (**PfEMP1**). We studied transcription of **var** genes (that encode **PfEMP1**) in placental parasites by amplifying and sequencing DBL.gamma. fragments from genomic DNA and cDNA of field isolates collected in western Kenya. We amplified DBL.gamma. fragments with divergent sequences from individual isolates by using various sequence-specific or degenerate primers. Transcripts detected with degenerate primers clustered phylogenetically within two DBL.gamma. subtypes with homol. to chr5_1.gen_150 or **FCR3**.varCSA. Interestingly, the DBL.alpha. encoded by chr5_1.gen_150 was recently found to be commonly expressed by placental isolates from Malawi. The findings are consistent with earlier serol. evidence that surface antigens of placental parasites have conserved features, and suggest that vaccines based on DBL.gamma. may only need to target a limited no. of variants.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:657318 HCAPLUS
DOCUMENT NUMBER: 130:37192
TITLE: Antigenic variation in malaria: in situ switching, relaxed and mutually exclusive transcription of var genes during intra-erythrocytic development in Plasmodium falciparum
AUTHOR(S): Scherf, A.; Hernandez-Rivas, R.; Buffet, P.; Bottius, E.; Benatar, C.; Pouvelle, B.; Gysin, J.; Lanzer, M.
CORPORATE SOURCE: Unite de Biologie des Interactions Hote-Parasite, CNRS URA 1960, Institut Pasteur, Paris, 75724, Fr.
SOURCE: EMBO Journal (1998), 17(18), 5418-5426
CODEN: EMJODG; ISSN: 0261-4189
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Members of the Plasmodium falciparum var gene family encode clonally variant adhesins, which play an important role in the pathogenicity of tropical malaria. Here the authors employ a selective panning protocol to generate isogenic P.falciparum populations with defined adhesive phenotypes for CD36, ICAM-1 and CSA (chondroitin sulfate A), expressing single and distinct var gene variants. This technique has established the framework for examg. var gene expression, its regulation and switching. It was found that var gene switching occurs in situ. Ubiquitous transcription of all var gene variants appears to occur in early ring stages. However, var gene expression is tightly regulated in trophozoites and is exerted through a silencing mechanism. Transcriptional control is mutually exclusive in parasites that express defined adhesive phenotypes. In situ var gene switching is apparently mediated at the level of transcriptional initiation, as demonstrated by nuclear run-on analyses.

The authors' results suggest that an epigenetic mechanism(s) is involved in var gene regulation.

IT **216493-18-4**
RL: PRP (Properties)
(amino acid sequence; antigenic variation in malaria: in situ switching, relaxed and mutually exclusive transcription of var genes during intra-erythrocytic development in Plasmodium falciparum)

IT **216654-44-3**
RL: PRP (Properties)
(nucleotide sequence; antigenic variation in malaria: in situ switching, relaxed and mutually exclusive transcription of var genes during intra-erythrocytic development in Plasmodium falciparum)

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L1 10 SEA FILE=REGISTRY ("PLASMODIUM FALCIPARUM ASPARAGINE-RICH PROTEIN (PLASMODIUM FALCIPARUM STRAIN 3D7 GENE MAL13P1.63)"/CN OR "PLASMODIUM FALCIPARUM CIRCUMSPOROZOITE HELPER T CELL EPITOPE"/CN OR "PLASMODIUM FALCIPARUM ERYTHROCYTE MEMBRANE PROTEIN"/CN OR "PLASMODIUM FALCIPARUM GAMETE ANTIGEN 27/25 (PLASMODIUM FALCIPARUM STRAIN 3D7 GENE PF13_0011)"/CN OR "PLASMODIUM FALCIPARUM MEMBRANE PROTEIN PF12 PRECURSOR (PLASMODIUM FALCIPARUM STRAIN 3D7 GENE MAL6P1.299)"/CN OR "PLASMODIUM FALCIPARUM MSP8-LIKE PROTEIN (PLASMODIUM FALCIPARUM STRAIN 3D7 GENE MAL6P1.221)"/CN OR "PLASMODIUM FALCIPARUM PROTEIN KINASE (PLASMODIUM FALCIPARUM STRAIN 3D7 CLONE MAL4P3 GENE PFD0740W)"/CN OR "PLASMODIUM FALCIPARUM RETICULOCYTE BINDING PROTEIN 2 B (PLASMODIUM FALCIPARUM STRAIN 3D7 GENE MAL13P1.176)"/CN OR "PLASMODIUM FALCIPARUM TROPHOZOITE ANTIGEN R45-LIKE PROTEIN (PLASMODIUM FALCIPARUM STRAIN 3D7 CLONE MAL4P4 GENE PFD1175W)"/CN OR "PLASMODIUM KNOWLESI ACID ENDOPEPTIDASE"/CN OR "PLASMODIUM-SPECIFIC HYDROPHOBIC ABUNDANT PROTEIN (PHYSARUM POLYCEPHALUM CLONE GLAV1-1 PRECURSOR)"/CN)
L2 7 SEA FILE=REGISTRY "PFEMP-1, TRUNCATED (PLASMODIUM FALCIPARUM STRAIN 3D7 GENE PF10-0385)"/CN OR ("PFEMP1 (PLASMODIUM FALCIPARUM GENE PFB0020C)"/CN OR "PFEMP1 (PLASMODIUM FALCIPARUM GENE PFB0045C)"/CN OR "PFEMP1 (PLASMODIUM FALCIPARUM GENE PFB1055C)"/CN OR "PFEMP1 FRAGMENT (PLASMODIUM FALCIPARUM GENE PFB1045W)"/CN OR "PFEMP1-LIKE PROTEIN (PLASMODIUM FALCIPARUM STRAIN 3D7 GENE MAL6P1.312)"/CN OR "PFEMP1-LIKE PROTEIN, TRUNCATED (PLASMODIUM FALCIPARUM STRAIN 3D7 GENE MAL6P1.312)"/CN)
L3 11 SEA FILE=REGISTRY CHONDROITIN SULFATE A?/CN
L4 2 SEA FILE=REGISTRY FCR3(L)VAR(L)CSA
L5 147 SEA FILE=HCAPLUS L1 OR L2 OR PLASMODIUM(W)FALCIPARUM(W)ERYTHROCYTE(W)MEMBRANE(W)PROTEIN OR PFEMP1 OR PFEMP(W)1
L6 9626 SEA FILE=HCAPLUS L3 OR CHONDROITIN(W)SULFATE(W)A OR CSA
L7 3 SEA FILE=HCAPLUS L4 OR FCR3(L)VAR(L)CSA
L8 17 SEA FILE=HCAPLUS L5 (L)BIND? AND L6
L9 3 SEA FILE=HCAPLUS L5 AND L7
L10 15 SEA FILE=HCAPLUS L8 NOT L9

=> d ibib abs hitrn l10 1-15

L10 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:576352 HCAPLUS

DOCUMENT NUMBER: 137:261039
TITLE: Molecular basis for the dichotomy in Plasmodium falciparum adhesion to CD36 and **chondroitin sulfate A**
AUTHOR(S): Gamain, Benoit; Gratepanche, Sylvie; Miller, Louis H.; Baruch, Dror I.
CORPORATE SOURCE: Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2002), 99(15), 10020-10024
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Plasmodium falciparum-infected erythrocytes adhere dichotomously to the host receptors CD36 and **chondroitin sulfate A** (**CSA**). This dichotomy is assocd. with parasite sequestration to microvasculature beds (CD36) or placenta (**CSA**), leading to site-specific pathogenesis. Both properties are mediated by members of the variant P. falciparum erythrocyte membrane protein 1 (**PfEMP-1**) family and reside on nonoverlapping domains of the mol. To identify the mol. basis for the apparent dichotomy, we expressed various domains of **PfEMP-1** individually or in combination and tested their **binding** properties. We found that the CD36-**binding** mode of the cysteine-rich interdomain region-1 (CIDR1) ablates the ability of the Duffy **binding**-like .gamma. domain to **bind CSA**. In contrast, neither a non-CD36-**binding** CIDR1 nor an intercellular adhesion mol. 1 **binding** domain had any affect on **CSA binding**. Our findings point out that interactions between different domains of **PfEMP-1** can alter the adhesion phenotype of infected erythrocytes and provide a mol. basis for the apparent dichotomy in adhesion. We suggest that the basis for the dichotomy is structural and that mutually exclusive conformations of **PfEMP-1** are involved in **binding** to CD36 or **CSA**. Furthermore, we propose a model explaining the requirement for structural dichotomy between placental and nonplacental isolates.

IT **24967-93-9, Chondroitin sulfate A**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mol. basis for the dichotomy in Plasmodium falciparum adhesion to CD36 and **chondroitin sulfate A**)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:369608 HCAPLUS
DOCUMENT NUMBER: 137:321068
TITLE: Identification of a conserved Plasmodium falciparum var gene implicated in malaria in pregnancy
AUTHOR(S): Rowe, J. Alexandra; Kyes, Sue A.; Rogerson, Stephen J.; Babiker, Hamza A.; Raza, Ahmed
CORPORATE SOURCE: Institute of Cell, Animal, and Population Biology, University of Edinburgh, Edinburgh, EH9 3JT, UK
SOURCE: Journal of Infectious Diseases (2002), 185(8), 1207-1211
CODEN: JIDIAQ; ISSN: 0022-1899
PUBLISHER: University of Chicago Press
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The **Plasmodium falciparum erythrocyte membrane protein** 1 (**PfEMP1**) family is a highly polymorphic class of variant surface antigens encoded by var genes that play an important role in malaria pathogenesis. This report describes the unexpected finding that 1 of the var genes encoding a **PfEMP1** variant that **binds** to the host receptor **chondroitin sulfate A** (**CSA**) and is implicated in malaria in pregnancy is well conserved among P. falciparum isolates worldwide. The N-terminal domains of this **PfEMP1** variant are esp. highly conserved, whereas the functional **CSA binding** domain is more variable. Anal. of var gene expression in placental parasites from primigravid women in Malawi did not support a role for this conserved gene in placental infection but identified a second commonly occurring var gene. These results indicate the need for reevaluation of previous assumptions of a minimal overlap between var gene repertoires from different parasite isolates.

IT **24967-93-9, Chondroitin sulfate A**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(an erythrocyte membrane protein 1 (EMP1) binds to; identification of a conserved Plasmodium falciparum var gene implicated in malaria in pregnancy)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:267526 HCAPLUS
DOCUMENT NUMBER: 137:152168
TITLE: Transcription of multiple var genes by individual, trophozoite-stage Plasmodium falciparum cells expressing a chondroitin sulphate A binding phenotype
AUTHOR(S): Duffy, Michael F.; Brown, Graham V.; Basuki, Wanny; Krejany, Efrosinia O.; Noviyanti, Rintis; Cowman, Alan F.; Reeder, John C.
CORPORATE SOURCE: Eijkman Institute for Molecular Biology, Australian Indonesia Medical Research Initiative (AusAID), Djakarta, 10430, Indonesia
SOURCE: Molecular Microbiology (2002), 43(5), 1285-1293
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this study, we detected multiple var gene transcripts within single, mature trophozoite-infected red blood cells (iRBCs) bound to **chondroitin sulfate A** (**CSA**). Several of the var detected had previously been demonstrated to encode Plasmodium falciparum erythrocyte membrane protein-1 (PfEMP-1) variants with domains that mediated iRBC adhesion to receptors other than **CSA**. Parasites expressing the **CSA**-adherent phenotype transcribed far more of one var than of all others, but this gene was different from the two other var previously purported to encode adhesion to **CSA**. Previous work suggesting that only single var are transcribed by mature trophozoites needs re-examn. in the light of these data from single, infected cells.

IT **24967-93-9, Chondroitin sulfate A**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(adhesion phenotype of infected erythrocytes; expression of multiple **PfEMP**-1/var gene transcripts by trophozoite-stage cells in erythrocytes expressing a **chondroitin**

sulfate A binding phenotype)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:704139 HCAPLUS
DOCUMENT NUMBER: 136:4454
TITLE: Role of nonimmune IgG bound to PfEMP1 in placental malaria
AUTHOR(S): Flick, Kirsten; Scholander, Carin; Chen, Qijun; Fernandez, Victor; Pouvelle, Bruno; Gysin, Jurg; Wahlgren, Mats
CORPORATE SOURCE: Microbiology Tumor Biology Center, Karolinska Inst., Stockholm, S-171 77, Swed.
SOURCE: Science (Washington, DC, United States) (2001), 293(5537), 2098-2100
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Infections with Plasmodium falciparum during pregnancy lead to the accumulation of parasitized red blood cells (infected erythrocytes, IEs) in the placenta. IEs of P. falciparum isolates that infect the human placenta were found to **bind** IgG. A strain of P. falciparum cloned for IgG **binding** adhered massively to placental syncytiotrophoblasts in a pattern similar to that of natural infections. Adherence was inhibited by IgG-**binding** proteins, but not by glycosaminoglycans or enzymic digestion of **chondroitin sulfate A** or hyaluronic acid. Normal, nonimmune IgG that is bound to a Duffy **binding**-like domain .beta. of the P. falciparum erythrocyte membrane protein 1 (**PfEMP1**) might at the IE surface act as a bridge to neonatal Fc receptors of the placenta.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:379906 HCAPLUS
DOCUMENT NUMBER: 135:151487
TITLE: Modifications in the CD36 binding domain of the Plasmodium falciparum variant antigen are responsible for the inability of **chondroitin sulfate A** adherent parasites to bind CD36
AUTHOR(S): Gamain, Benoit; Smith, Joseph D.; Miller, Louis H.; Baruch, Dror I.
CORPORATE SOURCE: Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Blood (2001), 97(10), 3268-3274
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adhesion of mature P. falciparum parasitized erythrocytes to microvascular endothelial cells or to placenta contributes directly to the virulence and severe pathol. of P. falciparum malaria. Whereas CD36 is the major endothelial receptor for microvasculature sequestration, infected erythrocytes adhering in the placenta **bind chondroitin sulfate A** (**CSA**) but not CD36. **Binding**

to both receptors is mediated by different members of the large and diverse protein family P. falciparum erythrocyte membrane protein-1 (**PfEMP-1**) and involves different regions of the mol. The **PfEMP-1-binding** domain for CD36 resides in the cysteine-rich interdomain region 1 (CIDR-1). To explore why **CSA** -**binding** parasites do not **bind** CD36, CIDR-1 domains from CD36- or **CSA-binding** parasites were expressed in mammalian cells and tested for adhesion. Although CIDR-1 domains from CD36-adherent strains strongly bound CD36, those from **CSA** -adherent parasites did not. The CIDR-1 domain has also been reported to **bind CSA**. However, none of the CIDR-1 domains tested bound **CSA**. Chimeric proteins between CIDR-1 domains that **bind** or do not **bind** CD36 and mutagenesis expts. revealed that modifications in the minimal CD36-**binding** region (M2 region) are responsible for the inability of **CSA**-selected parasites to **bind** CD36. One of these modifications, mapped to a 3-amino acid substitution in the M2 region, ablated **binding** in one variant and largely reduced **binding** of another. These findings provide a mol. explanation for the inability of placental sequestered parasites to **bind** CD36 and provide addnl. insight into crit. residues for the CIDR-1/CD36 interaction.

IT **24967-93-9, Chondroitin sulfate A**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(modifications in CD36 **binding** domain of Plasmodium falciparum antigen **PfEMP-1** are responsible for inability of **chondroitin sulfate A** adherent parasites to **bind** CD36)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:283442 HCAPLUS
DOCUMENT NUMBER: 135:255364
TITLE: Variants of Plasmodium falciparum erythrocyte membrane protein 1 expressed by different placental parasites are closely related and adhere to **chondroitin sulfate A**
AUTHOR(S): Khattab, Ayman; Kun, Jurgen; Deloron, Philippe; Kremsner, Peter G.; Klinkert, Mo-Quen
CORPORATE SOURCE: Department of Parasitology, University of Tubingen, Tubingen, 72074, Germany
SOURCE: Journal of Infectious Diseases (2001), 183(7), 1165-1169
CODEN: JIDIAQ; ISSN: 0022-1899
PUBLISHER: University of Chicago Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Plasmodium falciparum-infected erythrocytes adhere to syncytiotrophoblast cells lining the placenta via glycosaminoglycans, such as **chondroitin sulfate A** (**CSA**) and hyaluronic acid. Adherence of infected erythrocytes to host receptors is mediated by P. falciparum erythrocyte membrane protein-1 (**PfEMP-1**). A single **PfEMP-1** domain (duffy **binding**-like [DBL]-3, of the .gamma. sequence class) from lab.-adapted strains is thought to be responsible for **binding** to **CSA**. In this study, DBL-.gamma. domains expressed by placental P. falciparum isolates were shown to have an affinity to **CSA**. All parasite populations accumulating in infected placentas express only 1

variant of **PfEMP-1**, each of which contains a DBL-.gamma. domain with **CSA binding** capacities. Furthermore, sequence anal. data provide evidence for antigenic conservation among the DBL-.gamma. sequences expressed by different placental parasites. This study offers a close reflection of the process of parasite adhesion in the placenta and is crucial to the understanding of the pathogenesis of malaria during pregnancy.

IT **24967-93-9, Chondroitin sulfate A**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(variants of Plasmodium falciparum erythrocyte membrane protein 1 expressed by different placental parasites are closely related and adhere to **chondroitin sulfate A**)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:244814 HCAPLUS
DOCUMENT NUMBER: 135:18218
TITLE: Molecular mechanisms of Plasmodium falciparum placental adhesion
AUTHOR(S): Scherf, Artur; Pouvelle, Bruno; Buffet, Pierre A.; Gysin, Jurg
CORPORATE SOURCE: Unite de Biologie des Interactions Hote-Parasite, CNRS URA 1960, Institut Pasteur, Paris, 75724, Fr.
SOURCE: Cellular Microbiology (2001), 3(3), 125-131
CODEN: CEMIF5; ISSN: 1462-5814
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 50 refs. In natural P. falciparum infections, parasitized erythrocytes (PEs) circulate in the peripheral blood for a period corresponding roughly to the first part of the erythrocytic life cycle (ring stage). Later, in blood-stage development, parasite-encoded adhesion mols. are inserted into the erythrocyte membrane, preventing the circulation of the PEs. The principal mol. mediating PE adhesion is P. falciparum erythrocyte membrane protein 1 (**PfEMP1**), encoded by the polymorphic var gene family. The population of parasites is subject to clonal antigenic variation through changes in var expression, and a single **PfEMP1** variant is expressed at the PE surface in a mutually exclusive manner. In addn. to its role in immune evasion, switches in **PfEMP1** expression may be assocd. with fundamental changes in parasite tissue tropism in malaria patients. A switch from CD36 **binding** to **chondroitin sulfate A** (**CSA**) **binding** may lead to extensive sequestration of PEs in placenta syncytiotrophoblasts. This is probably a key event in malaria pathogenesis during pregnancy. The **CSA-binding** phenotype of mature PEs is linked to another distinct adhesive phenotype: the recently described **CSA**-independent cytoadhesion of ring-stage PEs. Thus, a subpopulation of PEs that sequentially displays these 2 different phenotypes may **bind** to an individual endothelial cell or syncytiotrophoblast throughout the asexual blood-stage cycle. This suggests that non-circulating (cryptic) parasite subpopulations are present in malaria patients.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:804208 HCAPLUS

DOCUMENT NUMBER: 134:54760
TITLE: Cytoadhesion of Plasmodium falciparum ring-stage-infected erythrocytes
AUTHOR(S): Pouvelle, B.; Buffet, P. A.; Lepolard, C.; Scherf, A.; Gysin, J.
CORPORATE SOURCE: Laboratoire de Parasitologie Experimentale, Faculte de Medecine, Universite de la Mediterranee, Marseille, 13385, Fr.
SOURCE: Nature Medicine (New York) (2000), 6(11), 1264-1268
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature America Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A common pathol. characteristic of Plasmodium falciparum infection is the cytoadhesion of mature-stage-infected erythrocytes (IE) to host endothelium and syncytiotrophoblasts. Massive accumulation of IE in the brain microvasculature or placenta is strongly correlated with severe forms of malaria. Extensive **binding** of IE to placental **chondroitin sulfate A** (**CSA**) is assocd. with physiopathol. during pregnancy. The adhesive phenotype of IE correlates with the appearance of **Plasmodium falciparum erythrocyte membrane protein** 1 (**PfEMP1**) at the erythrocyte surface (approx. 16 h after merozoite invasion), so that only early blood-stage (ring-stage) IE appear in the peripheral blood. Here, we describe results that challenge the existing view of blood-stage IE biol. by demonstrating the specific adhesion of IE, during the early ring-stage, to endothelial cell lines from the brain and lung and to placental syncytiotrophoblasts. Later, during blood-stage development of these IE, trophozoites switch to an exclusively **CSA** cytoadhesion phenotype. Therefore, adhesion to an individual endothelial cell or syncytiotrophoblasts may occur throughout the blood-stage cycle, indicating the presence in malaria patients of noncirculating (cryptic) parasite subpopulations. We detected two previously unknown parasite proteins on the surface of ring-stage IE. These proteins disappear shortly after the start of **PfEMP1**-mediated adhesion.

IT **24967-93-9, Chondroitin sulfate A**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cytoadhesion of Plasmodium falciparum ring-stage-infected erythrocytes, in humans)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:504129 HCAPLUS
DOCUMENT NUMBER: 134:221093
TITLE: Plasmodium falciparum: Cloned and Expressed CIDR Domains of **PfEMP1 Bind** to **Chondroitin Sulfate A**
AUTHOR(S): Degen, Roland; Weiss, Niklaus; Beck, Hans-Peter
CORPORATE SOURCE: Swiss Tropical Institute, Basel, CH 4002, Switz.
SOURCE: Experimental Parasitology (2000), 95(2), 113-121
CODEN: EXPAAA; ISSN: 0014-4894
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Adherence of erythrocytes infected with mature asexual P. falciparum parasites (iRBC) to microvascular endothelial cells contributes to the pathol. of P. falciparum malaria. It has been shown that the variant P.

falciparum erythrocyte membrane protein 1 (**PfEMP1**) confers adhesion to a wide range of cell surface receptors. Previously, the cysteine-rich interdomain region (CIDR) of **PfEMP1** has been identified as **binding** site to CD36. The authors provide evidence that the same region can also mediate **binding** to **chondroitin sulfate A** (**CSA**). CIDR domains of two different parasite strains were expressed in Escherichia coli as a 6xHis-tagged protein. Purified recombinant protein bound to Chinese hamster ovary (CHO) cells which naturally express **chondroitin sulfate A**. Treatment of wild-type CHO cells with chondroitinase ABC reduced **binding** up to 94.4%. Competitive **binding** using sol. **CSA** inhibited **binding** to CHO cells by up to 100% at 2 mg/mL and by 62.4% at 0.5 mg/mL, whereas 1 mg/mL heparan sulfate had only a little effect (18.1%). In contrast, a recombinant 6xHis-tagged DBL1 domain showed no **binding** to wild-type CHO cells. Such an approach of analyzing various domains of **PfEMP1** as recombinant proteins may elucidate their functions and may lead to novel anti-adherence therapeutics, esp. for maternal malaria infections. (c) 2000 Academic Press.

IT **24967-93-9, Chondroitin sulfate A**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(Plasmodium falciparum CIDR domains of **PfEMP1 binding** to **chondroitin sulfate A**)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:438436 HCAPLUS
DOCUMENT NUMBER: 133:173557
TITLE: Identification of glycosaminoglycan **binding** domains in **Plasmodium falciparum erythrocyte membrane protein** 1 of a **chondroitin sulfate A**-adherent parasite
AUTHOR(S): Reeder, John C.; Hodder, Anthony N.; Beeson, James G.; Brown, Graham V.
CORPORATE SOURCE: Walter and Eliza Hall Institute of Medical Research, Parkville, 3050, Australia
SOURCE: Infection and Immunity (2000), 68(7), 3923-3926
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Accumulation of Plasmodium falciparum-infected erythrocytes in the placenta is a key feature of maternal malaria. This process is mediated in part by the parasite ligand P. falciparum erythrocyte membrane protein 1 (**PfEMP1**) at the surface of the infected erythrocyte interacting with the host receptor **chondroitin sulfate A** (**CSA**) on the placental lining. We have localized **CSA binding** activity to two adjacent domains in **PfEMP1** of an adherent parasite line and shown the presence of at least three active glycosaminoglycan **binding** sites. A putative **CSA binding** sequence was identified in one domain, but nonlinear **binding** motifs are also likely to be present, since **binding** activity in the region was shown to be dependent on conformation. Characterization of this **binding** region provides an opportunity to investigate further its potential as a target for antiadhesion therapy.

IT **24967-93-9, Chondroitin sulfate A**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(identification of glycosaminoglycan-**binding** domains in **Plasmodium falciparum erythrocyte membrane protein** 1 of a **chondroitin sulfate A**-adherent parasite)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:379143 HCAPLUS
DOCUMENT NUMBER: 133:103071
TITLE: The Duffy-**binding**-like domain 1 of **Plasmodium falciparum erythrocyte membrane protein** 1 (**PfEMP1**) is a heparan sulfate ligand that requires 12 mers for **binding**
AUTHOR(S): Barragan, Antonio; Fernandez, Victor; Chen, Qijun; Von Euler, Anne; Wahlgren, Mats; Spillmann, Dorothe
CORPORATE SOURCE: Microbiology and Tumor Biology Center, Karolinska Institutet and Swedish Institute for Infectious Disease Control, Stockholm, S-171 77, Swed.
SOURCE: Blood (2000), 95(11), 3594-3599
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **Plasmodium falciparum erythrocyte membrane protein** 1 (**PfEMP1**), present on the surfaces of parasitized red blood cells (pRBC), mediates rosetting, a virulent phenotype. Here, we show that pRBC specifically **bind** heparan sulfate (HS) and heparin onto their surfaces and that the rosetting ligand **PfEMP1** specifically adheres to heparin-Sepharose when extd. from the surfaces of radioiodinated infected RBC. An anal. of the **binding** properties of the different regions of **PfEMP1** provides evidence that the Duffy-**binding**-like domain-1 (DBL-1) is the predominant ligand involved in HS and heparin **binding**. Sol. DBL-1 requires a minimal heparin fragment size of a 12-mer (.apprxeq.4 kd) for **binding** and is critically dependent on N-sulfation. A 12-mer is also the minimal heparin fragment that disrupts naturally formed rosettes. DBL-1 **binds** specifically to erythrocytes and also to HS from endothelial cells and human aorta but not to **chondroitin sulfate A**, suggesting that different PfEMP1s mediate adhesion to distinct glycosaminoglycans in individual malaria parasites. Present data suggest that HS on endothelial cells may also be involved in the sequestration of pRBC. Elucidation of these **binding** mechanisms opens up new possibilities for therapeutic strategies targeting adhesive interactions of pRBC.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:304104 HCAPLUS
DOCUMENT NUMBER: 133:131452
TITLE: Characterization of the chondroitin sulfate of Saimiri brain microvascular endothelial cells involved in Plasmodium falciparum cytoadhesion

AUTHOR(S): Fusai, T.; Parzy, D.; Spillmann, D.; Eustacchio, F.; Pouvelle, B.; Lepolard, C.; Scherf, A.; Gysin, J.
CORPORATE SOURCE: Unite de Parasitologie, IMTSSA, Marseille, 13007, Fr.
SOURCE: Molecular and Biochemical Parasitology (2000), 108(1), 25-37
CODEN: MBIPDP; ISSN: 0166-6851
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cytoadhesion of Plasmodium falciparum-infected erythrocytes (IRBC) to chondroitin-4-sulfate (**CSA**) is inhibited by sol. **CSA** in vitro on Saimiri brain microvascular endothelial cells (SBEC) and in vivo in P. falciparum-infected Saimiri monkeys. We tested whether the SBEC model was appropriate for studying **CSA-binding** IRBC using four cell lines. All SBEC expressed a chondroitin sulfate (CS), with a compn. of **CSA**. The mean sizes of these **CSA** were 20.5, 22, 23, 32.5 and 36 kDa for SBEC 3A and C2, CHO, SBEC 1D and 17, resp. We found that cytoadhesion of the Palo-Alto (FUP)1 **CSA -binding** phenotype, selected by panning on SBEC 17, was specifically inhibited in a dose-dependent manner by all the purified **CSA**. The extent of inhibition depended on the cellular origin of the tested **CSA**. SBEC 17 **CSA** was 33 times more efficient than CHO-**CSA** and 21 times more efficient than the 50 kDa com. bovine trachaea **CSA**. Dynabeads coated with a total ext. of SBEC 1D CS-proteoglycans interacted with **CSA**- but not with CD36- or ICAM-1-**binding** IRBC. These Dynabeads also interacted specifically with the **PfEMP1** DBL-3 domain, on the surface of CHO transfectants, but not with the CIDR-1 domain. Thrombomodulin was involved in IRBC adhesion to all SBEC whereas CD44 was only expressed by SBEC 1D and 17. These two **CSA**-proteoglycans have also been detected at the surface of human endothelial cells. Thus, the two homologous models, SBEC/Saimiri sciureus, are useful and reliable tools for the evaluation of new anti-**CSA** adhesion treatments and anti-disease vaccines for pregnant women.

IT **24967-93-9**, Chondroitin 4-sulfate
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(characterization of chondroitin sulfate of Saimiri brain microvascular endothelial cells involved in Plasmodium falciparum cytoadhesion)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:728934 HCAPLUS
DOCUMENT NUMBER: 132:62480
TITLE: Plasmodium falciparum domain mediating adhesion to **chondroitin sulfate A**: a receptor for human placental infection
AUTHOR(S): Buffet, Pierre A.; Gamain, Benoit; Scheidig, Christine; Baruch, Dror; Smith, Joseph D.; Hernandez-Rivas, Rosaura; Pouvelle, Bruno; Oishi, Shinya; Fujii, Nobutaka; Fusai, Thierry; Parzy, Daniel; Miller, Louis H.; Gysin, Jurg; Scherf, Artur
CORPORATE SOURCE: Unite de Biologie des Interactions Hote-Parasite, Centre National de la Recherche Scientifique/Unite de Recherche Associee 1960, Institut Pasteur, Paris, 75724, Fr.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(22), 12743-12748

CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Malaria during the first pregnancy causes a high rate of fetal and neonatal death. The decreasing susceptibility during subsequent pregnancies correlates with acquisition of antibodies that block **binding** of infected red cells to **chondroitin sulfate A** (**CSA**), a receptor for parasites in the placenta. Here the authors identify a domain within a particular **Plasmodium falciparum erythrocyte membrane protein** 1 that **binds CSA.** The authors cloned a var gene expressed in **CSA-binding** parasitized red blood cells (PRBCs). The gene had eight receptor-like domains, each of which was expressed on the surface of Chinese hamster ovary cells and was tested for **CSA binding.** **CSA** linked to biotin used as a probe demonstrated that two Duffy-**binding**-like (DBL) domains (DBL3 and DBL7) bound **CSA.** DBL7, but not DBL3, also bound chondroitin sulfate C (CSC) linked to biotin, a neg. charged sugar that does not support PRBC adhesion. Furthermore, **CSA,** but not CSC, blocked the interaction with DBL3; both **CSA** and CSC blocked **binding** to DBL7. Thus, only the DBL3 domain displays the same **binding** specificity as PRBCs. Because protective antibodies present after pregnancy block **binding** to **CSA** of parasites from different parts of the world, DBL-3, although variant, may induce cross-reactive immunity that will protect pregnant women and their fetuses.

IT **24967-93-9, Chondroitin sulfate A**
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Plasmodium falciparum domain mediating adhesion to **chondroitin sulfate A**: a receptor for human placental infection)

IT **253135-44-3**
RL: PRP (Properties)
(amino acid sequence; Plasmodium falciparum domain mediating adhesion to **chondroitin sulfate A**: a receptor for human placental infection)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:306573 HCAPLUS
DOCUMENT NUMBER: 131:100700
TITLE: The adhesion of Plasmodium falciparum-infected erythrocytes to **chondroitin sulfate A** is mediated by P. falciparum erythrocyte membrane protein 1
AUTHOR(S): Reeder, John C.; Cowman, Alan F.; Davern, Kathleen M.; Beeson, James G.; Thompson, Jennifer K.; Rogerson, Stephen J.; Brown, Graham V.
CORPORATE SOURCE: The Walter and Eliza Hall Institute of Medical Research, Post Office Royal Melbourne Hospital, Victoria, 3050, Australia
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(9), 5198-5202
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Chondroitin sulfate A** (**CSA**) is an important receptor for the sequestration of Plasmodium falciparum in the placenta, but the parasite ligand involved in adhesion has not previously been identified. Here the authors report the identification of a var gene transcribed in assocn. with binding to **CSA** and present evidence that the P. falciparum erythrocyte membrane protein 1 product of the gene is the parasite ligand mediating **CSA** binding. Description of this gene and the implication of P. falciparum erythrocyte membrane protein 1 as the parasite ligand paves the way to a more detailed understanding of the pathogenesis of placental infection and potential therapeutic strategies targeting the interaction.

IT **24967-93-9, Chondroitin sulfate A**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**Plasmodium falciparum erythrocyte membrane protein** 1 encoded by var gene sequence and role as parasite ligand in **binding** to **chondroitin sulfate A** on erythrocytes)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:663609 HCAPLUS
DOCUMENT NUMBER: 130:20241
TITLE: A recombinant peptide based on PfEMP-1 blocks and reverses adhesion of malaria-infected red blood cells to CD36 under flow
AUTHOR(S): Cooke, Brian M.; Nicoll, Claire L.; Baruch, Dror I.; Coppel, Ross L.
CORPORATE SOURCE: Department of Microbiology, Monash University, Clayton, 3168, Australia
SOURCE: Molecular Microbiology (1998), 30(1), 83-90
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB During falciparum malaria infection, severe complications ensue because parasitized red blood cells (PRBCs) adhere to endothelial cells and accumulate in the microvasculature. At the mol. level, adhesion is mediated by interaction of **Plasmodium falciparum erythrocyte membrane protein** 1 (**PfEMP -1**) on the PRBC surface with receptors on the surface of endothelial cells, including CD36. The authors have shown that a recombinant 179-residue subfragment of **PfEMP-1** (rC1-2[1-179]), which encompasses the CD36-**binding** region, inhibits and reverses adhesion of PRBCs to CD36 under physiol. relevant flow conditions. RC1-2[1-179] inhibited adhesion in a concn.-dependent manner over the range 100 pM to 2 .mu.M, with .ltoreq.99% of adhesion blocked at the highest concn. tested. The antiadhesive activity of rC1-2[1-179] was not strain specific and almost totally ablated adhesion of four different parasite lines. Furthermore, rC1-2[1-179] showed remarkable ability to progressively reverse adhesion when flowed over adherent PRBCs for 2 h. The effect of rC1-2[1-179] was, however, specific for CD36-mediated adhesion and had no effect on adhesion mediated by **CSA**. Interference with **binding** of PRBCs to the vascular endothelium using rC1-2[1-179] or smaller org. mimetics may be a useful therapeutic approach to ameliorate severe complications of falciparum malaria.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT